

Frequently Asked Questions and Answers for Tobacco Regulatory Science R01: Abuse Liability Associated with Reduced Nicotine Content Tobacco Products

[RFA-OD-15-006](#)

Updated October 26, 2015

ELIGIBLE APPLICANTS

1. Are foreign institutions eligible to apply?
 - A. Yes, foreign institutions are eligible to apply including “Non-domestic (non-U.S.) Entities (Foreign Institutions), Non-domestic (non U.S.) components of U.S Organizations, and Foreign Components, as defined by the [NIH Grants Policy Statement](#).” NIH grants policy does not prohibit a foreign for-profit institution from applying for this funding opportunity announcement ([FOA](#)). However, foreign applicants must demonstrate that the proposed research is not possible to pursue domestically and that it can directly contribute to the U.S. FDA’s regulatory authority over the manufacture, marketing and distribution of tobacco products (see Q&A #10).
2. Are tobacco companies eligible to apply to this funding opportunity?
 - A. Yes. As stated in the funding opportunity announcement, for-profit organizations are eligible to apply. It is the responsibility of the NIH peer review and council recommendations to identify the merit and quality of applications, as well as FDA’s consideration of the relevance of the application to program priorities, to determine the entity’s success in securing funding for research.

BUDGET

3. Are modular budgets acceptable?
 - A. No, modular budgets will not be accepted regardless of total costs. Detailed budgets must be submitted.
4. Is there a budget cap on applications submitted in response to this FOA?
 - A. Yes. Applications submitted to this funding announcement are limited to budgets of no more than \$500,000 in direct costs per year.

APPLICATION SUBMISSION

5. Should applications be submitted electronically or through paper?
 - A. Applications must be submitted electronically. Applicants should follow the instructions in the [SF424 \(R&R\) Application Guide](#), including [Supplemental Grant Application Instructions](#) except where instructed in this funding opportunity announcement to do otherwise.

6. Am I required to submit a letter of intent?
- A. A letter of intent is not required, and it does not enter into the review process. However, it allows for NIH staff to estimate the potential review workload and plan the review. Investigators are encouraged to communicate with [NIH scientific contacts](#) to discuss their research ideas and specific aims prior to submitting applications, as all proposed research-specific aims must be within the regulatory authority of the FDA CTP in order to be deemed responsive to this FOA. Applications that are nonresponsive will not be reviewed.

Suggested content of letter of intent:

- Descriptive title of proposed activity
- Name(s), address(es), and telephone number (s) of the PD(s)/PI(s)
- Names of other key personnel
- Participating institution(s)
- Number and title of this funding opportunity
- Specific Aims

7. Where do I send the letter of intent?
- A. The letter may be sent by email to: TRSP@mail.nih.gov

Or by regular mail to:

Tobacco Regulatory Science Program
Office of Disease Prevention
6100 Executive Boulevard
Room 3B01, MSC 7530
Bethesda, MD 20892-7530 (Use Rockville, MD 20852 for Express Mail)
Tel: 301-451-7464
Fax: 301-480-2230

PAGE LIMITATIONS

8. Does the application have a page limit?
- A. Yes. All page limitations described in the SF424 Application Guide and the [Table of Page Limits](#) must be followed.

RESEARCH OBJECTIVES, SCOPE AND RESPONSIVENESS

9. How do I know if my application is responsive to this [funding opportunity announcement \(FOA\)](#)?
- A. This is a critical question, as *each of the specific aims* in the application must meet the following criteria to be considered responsive:
- address one or more of the 3 interest areas listed in the [FOA](#).
 - fall within scope of FDA CTP's regulatory authority.

As such, applicants are strongly encouraged to contact the [scientific research contacts](#) listed in the [FOA](#) for feedback about responsiveness prior to submitting an application. Upon receipt, applications will be **evaluated for responsiveness** by the Food and Drug Administration (FDA) Center for Tobacco Products (CTP) and components of participating organizations, NIH. **Only applications that are within scope of the three areas listed in the [FOA](#) and FDA CTP's regulatory authority will be reviewed.**

Your application abstract and specific aims are used to make this determination, so it is important that you are clear about your proposed scientific aims and how they may potentially inform CTP's regulatory authority. Staff reviewing your application will not try to infer how your research falls within CTP's regulatory authority beyond what is stated in the abstract and specific aims. If your application is deemed responsive, it will undergo scientific peer review by experts convened specifically for this FOA (by the NIH Center for Scientific Review). If your application is deemed nonresponsive, it will be withdrawn prior to evaluation of its scientific merit, i.e., peer review.

10. FDA/CTP has regulatory authority over the manufacture, marketing and distribution of tobacco products. What are some examples of these authorities?

A. The Family Smoking Prevention and Tobacco Control Act gave FDA responsibility for and authority to, among other things:

- Restrict cigarettes and smokeless tobacco retail sales to youth.
- Restrict the sale and distribution of tobacco products, including advertising and promotion, as appropriate to protect public health.
- Review modified risk tobacco products, such as those marketed for use to reduce harm, prior to their introduction to the market.
- Adjust warning labels for cigarettes and smokeless tobacco products in order to promote greater public understanding of the risks of tobacco use.
- Establish standards for tobacco products (for example, setting limits on harmful and potentially harmful constituents and nicotine levels) as appropriate to protect the public health.
- Review new tobacco products prior to their introduction to the market.

For more information, see "Overview of the Family Smoking Prevention and Tobacco Control Act" at:

<http://www.fda.gov/downloads/TobaccoProducts/GuidanceComplianceRegulatoryInformation/UCM246207.pdf>

11. What are the research interest areas for this [funding opportunity announcement \(FOA\)](#)?

A. The purpose of this [FOA](#) is to generate data to inform the FDA on ways to reduce the addictiveness and resulting public health toll from tobacco product use in the United States. Research/findings should be applicable to the abuse liability of cigarettes and combusted tobacco products. *Only applications proposing research projects relevant to one or more of these areas will be considered for funding:*

1. Clinical abuse liability studies (e.g., behavioral economics, drug discrimination, self-administration, and dose-response studies) to evaluate the reinforcing and discriminative effects of varying, low doses of nicotine. Studies should include assessments of withdrawal, dependence, and initiation. Studies should be applicable to cigarettes and may include a variety of tobacco products (e.g., very low nicotine content cigarettes), other nicotine delivery methods, (e.g., IV nicotine administration), and diverse tobacco user populations (e.g., novice users, intermittent users, and established tobacco users).

2. Animal models of adolescent nicotine reinforcement (i.e., dose-response studies) and use behaviors, including animal models of initiation.

3. Studies examining the effects of reduced nicotine content tobacco products on dual/poly use and switching behaviors. Studies may address the appeal and potential for initiation with reduced nicotine content tobacco products in non-tobacco users, particularly adolescents and young adults.

12. Are the three research questions in the RFA listed in order of priority to FDA, or are they of equal priority?

A. The research questions are not listed in priority order. They are of equal priority to FDA CTP.

13. In general, what areas of research are **not within FDA CTP's regulatory authority**?

A. The Family Smoking Prevention and Tobacco Control Act gives FDA the authority to regulate the manufacture, marketing, and distribution of tobacco products to protect public health and to reduce tobacco use by youth. In general, CTP's regulatory authorities do NOT extend to the following:

- Setting tax rates for tobacco products.
- Regulating therapeutic products, such as those marketed to treat tobacco dependence.
- Setting clean indoor air polices.
- Regulating tobacco growing.

14. Is a treatment intervention study designed to compare the effectiveness of various tobacco products on tobacco cessation considered responsive?

A. No. CTP's regulatory authority does not extend to regulating therapeutic uses of tobacco products as this authority rests with other Centers within FDA. Examples of research projects that would be considered responsive include an observational study to examine the natural history of whether participants quit smoking cigarettes while using a different tobacco product, and assessing if communications regarding the health consequences of using tobacco products have an impact on usage rates.* In many of its key regulatory areas, CTP is charged with assessing the impact of tobacco products on the health of the population as a whole, taking into account both users of tobacco products and persons who do not currently use tobacco products as well as the increased or

decreased likelihood that existing users of tobacco products will stop using such products; and the increased or decreased likelihood that those who do not use tobacco products will start using such products.

**** The examples provided are illustrative and should not be viewed as definitive or comprehensive.***

15. Is a treatment intervention study designed to evaluate the effectiveness of a treatment for tobacco dependence (medications and/or behavioral counseling) on tobacco cessation considered responsive?

A. No. CTP's regulatory authority does not extend to evaluation of interventions designed to promote cessation. Although a section of the Tobacco Control Act addresses medications to treat tobacco dependence (Sec. 918), this section of the Tobacco Control Act is under the authority of FDA's Center for Drug Evaluation and Research.

**** The examples provided are illustrative and should not be viewed as definitive or comprehensive.***

16. Is a research proposal in which the primary outcome informs treatment of disease considered responsive?

A. No. CTP does not regulate products intended for the treatment of disease, for example, pharmacotherapy for treatment of cancer or emphysema or screening, physical activity or dietary interventions for heart disease. *

**** The examples provided are illustrative and should not be viewed as definitive or comprehensive.***

17. Is a research proposal in which the primary outcome identifies differential effects of various tobacco products on disease risk, incidence, or progression of disease considered responsive?*

A. Yes. This proposal identifying differential effects of various tobacco products on disease would be responsive. Examples* might include:

- pulmonary function testing outcomes following use of various combustible tobacco products
- oral manifestations following use of various tobacco products, especially new and emerging tobacco products.

**** The examples provided are illustrative and should not be viewed as definitive or comprehensive.***

18. What types of biomarker research may be appropriate for FDA CTP funding?

A. Proposals identifying biomarkers of specific tobacco product exposure and/or disease, and those with the potential to differentiate exposure of differing tobacco products could be considered responsive. Examples* include:

- Biomarkers to measure exposure to new and emerging tobacco products
- Biomarkers of disease (e.g., cancer, cardiovascular disease, pulmonary disease, reproductive and developmental effects) that can be associated with specific measures of tobacco exposure

- Development of a nonclinical biomarker of disease coupled to traditional toxicology and/or pharmacology studies to provide a relevant framework for the regulatory application
- Studies linking biomarkers of disease in nonclinical models that translate to biomarkers that are measurable in the clinical setting
- Magnitude of changes in biomarkers of disease that translates into clinically meaningful impacts on human health outcomes
- Novel biological and physiological markers (including genetic and epigenetic markers) that are predictive of smoking-related and smokeless tobacco-related adverse health outcomes.

Biomarker proposals in which the primary focus is to inform treatment would not be responsive.

**** The examples provided are illustrative and should not be viewed as definitive or comprehensive.***

19. What types of research on nicotine and/or nicotinic receptors are appropriate for consideration of funding by CTP?

- A. If the research provides information on outcomes such as motor activity, memory, or neuronal responses to particular ligands, the research is likely not appropriate. Research to rapidly screen tobacco constituents for activity at the nicotinic receptor to determine their dependence potential would be considered responsive.*

**** The examples provided are illustrative and should not be viewed as definitive or comprehensive.***

20. Are studies on the impact of state and local tobacco control policies responsive?

- A. It depends upon the specific policies being examined, and whether they fall under the purview of the FDA CTP. Studies evaluating the impact of a tobacco tax increase are not responsive, as CTP does not have regulatory authority regarding tax rates on tobacco products. Similarly, CTP does not have authority over the sale of tobacco cessation medications, so, for example, a study evaluating the effectiveness for tobacco cessation of providing free nicotine replacement therapy would not be considered responsive. Studies evaluating the impact of a tobacco advertising restriction, a ban on the sale of flavored tobacco products, or restrictions on the sale of single-serving products, however, may be considered responsive.*

**** The examples provided above are illustrative and should not be viewed as definitive or comprehensive.***

AWARD SELECTION

21. Will more weight be assigned in the review for applications that address more than 1 of the 3 priority areas?
- A. No. Reviewers will be looking to see if the research question is addressed adequately and appropriately. When approaching which research questions to answer, it is recommended that investigators think about what scientific evidence FDA would need to support a product review process or regulatory decision.
22. On what basis are applications selected for funding?
- A. Applications will be selected for funding based on scientific merit, current research priorities, availability of funds, and FDA CTP current research priorities.

POST-AWARD MANAGEMENT AND REPORTING

23. Which NIH Institute/Center (IC) will manage my award?
- A. It depends on the nature and scope of the research projects proposed. Applicants may request assignment to a particular Institute in their cover letter, but the NIH will make the final determination regarding Institute assignment.
24. Are the reporting requirements for these awards the same as other NIH grants?
- A. No. An Interim Report will be due every six (6) months following the project start date, as well as the annual progress report and all reports at the time of grant closeout. It is critical that CTP funds be used only to support research that is responsive to FDA's authority to regulate the manufacture, marketing, and distribution of tobacco products. Any proposed change in scope or specific aims requires pre-approval.
25. Are policies and procedures different for these awards?
- A. Yes. This includes exclusion from Streamlined Noncompeting Award Procedures (SNAP) and all carryover requests requiring prior approval.
26. Some researchers are under limitations with respect to accepting funds from the tobacco industry. How will these FDA research awards be funded?
- A. As mandated in the Tobacco Control Act, FDA is authorized to collect fees from tobacco product manufacturers and importers for its activities related to the regulation of the manufacture, distribution, and marketing of tobacco products. Although the tobacco user fees are specified in statute, Congress must actually appropriate the funds before FDA can obligate them. The tobacco industry has no control over CTP funding decisions. FDA uses some of these funds to award research grants.
27. What will be the availability of confidential information obtained by the FDA, for example, product and constituent reporting?
- A. Several laws govern the confidentiality of tobacco product information submitted to FDA, including sections 301(j) and 906(c) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), the Trade Secrets Act, and the Freedom of

Information Act, as well as FDA's implementing regulations. FDA's general regulations concerning the public availability of FDA records are contained in 21 CFR Part 20. Regarding the reporting of constituents, the FD&C Act requires tobacco product manufacturers and importers to report quantities of harmful and potentially harmful constituents (HPHCs) in tobacco products or tobacco smoke by brand and sub-brand. The FD&C Act also directs the Agency to publish a list of HPHCs by brand and by quantity in each brand and sub-brand, in a format that is understandable and not misleading to a layperson.

RESEARCH RESOURCES

28. If a scientific study proposes to make ANY change to a commercialized tobacco product (e.g., manipulating the size of the product; putting the tobacco product in different colored packaging), then an investigational tobacco products (ITP) request is recommended by FDA (Reference: [Draft Guidance Use of Investigational Tobacco Products](#)). What information is required in the ITP request?

A. The information needed in an ITP request may vary depending on the proposed ITP and the type of study. FDA needs to determine whether the product is a tobacco product, whether the tobacco product is within our current jurisdiction, whether the tobacco product is an ITP, and whether the study products will be provided to human subjects. For example, if one makes a change in labeling of a commercially marketed tobacco product and it will not be used by human subjects, no ITP request is needed. If one makes a change in labeling of a commercially marketed tobacco product and there will be actual use by human subjects, then FDA recommends that an ITP request come to CTP for review, but it is likely that chemistry, engineering, and manufacturing will not be needed. If you have questions about ITP, please contact Debbie Cordaro (debbie.cordaro@fda.hhs.gov).

29. Is there any guarantee that all strengths and varieties of reduced nicotine cigarettes will be made available by the NIDA Drug Supply Program?

A. Investigators are encouraged to consult with NIDA's Nicotine Research Cigarettes Drug Supply Program to determine availability of reduced nicotine cigarettes: <http://www.drugabuse.gov/nicotine-research-cigarette-drug-supply-program>.

NIH-FDA Tobacco Regulatory Science Program Web site: <http://prevention.nih.gov/tobacco/>